

January 23, 1954

Dear Luca:

Your letter of the 18th was on my desk this morning and leads to this instant reply. I cannot say how delighted Esther and I are at this good news! But I must admit that I would have been greatly surprised (as well as disappointed) if the Rockefeller Foundation had now refused your application after you had been given such encouragement.

The notion of a small book as an expansion of our symposium paper seems very practical. It would not be too soon to give some preliminary thought to its organization, though I am in complete agreement with your first suggestions. Why do we not soon each prepare a somewhat more detailed chapter outline to be exchanged for detailed comments? I agree that the kernel of the book should be adaptation to drugs, but that it would be advisable to surround this with diverse background material, including even drug-tolerance and drug-refractoriness in animals. I have yet to see an acceptable treatment of drug resistance in any textbook or monograph on the antibiotics, and my experience in lectures before physicians and internists actually involved in chemotherapeutic practice suggests a large audience equally dissatisfied with current treatments. I might add we now have a dictating machine in the department which should greatly facilitate our labors. Is there any chance of your finding access to an Edison Co. "Voicewriter" (disk, not cykinder, recordings)?

As to finances, \$325, tax-free, will be a comfortable but not luxurious stipend. If the Rockefeller Foundation is subsidizing your visit, it might be in poor taste for your ~~supplemental~~ stipend to be supplemented again from their own grant to us, and you would then have tax difficulties. However, if your wife has any sort of University qualification, it might be possible to arrange ~~some sort of position~~ a job for her. It will be essential for you to anticipate this when applying for your visa, but I believe there is no firm objection to employment of professional exchange visitors in direct connection with the purposes of their visit. But as I indicated, the \$325 is an adequate basis, and except for the visa question we can settle any other arrangements later.

As to housing, would you be willing to leave the matter in our hands? Surely you would prefer a small apartment, if not too expensive, to a simple room. You would save considerably in food costs! I think something suitable could be found for around \$90 per month, which is not inordinate in view of such savings, and compares with \$50-60 for the meanest sort of "light housekeeping" rooms. Let us know your wishes. If you would prefer to exercise your personal discretion, I am sure you will be able to find something at any time, but the choice will naturally be wider in advance.

As to research, this is rapidly moving to a climax in connection with the single cell studies, and your visit should coincide with the fulfillment of it. Recent efforts have been concentrated on validating the results from colony platings, which suggested that the primary hybrids (or their early progeny) from a cross of the type Hfr Lac<sup>+</sup> Gal<sup>-</sup> S<sup>+</sup> x F<sup>-</sup> Lac<sup>-</sup> Gal<sup>+</sup> S<sup>+</sup> might often contain the full Hfr-parental-complement as well as the F<sup>-</sup>-complement and the most frequent recombinant (Lac<sup>+</sup>Gal<sup>+</sup>S<sup>+</sup>). (Recombinants carrying S<sup>+</sup> have not yet been found, so this locus definitely stands in a unique position in re elimination.) This has at any rate been confirmed by the single cell isolations. Until today, 182 single cells have been isolated from cross mix-

tures. Some of these were at random (usually from 1-3 hour mixtures); in others, I tried to isolate what I thought might be zygote cells: rather larger cells, or cells from pairs. Of the total 182, 11 have been interesting (i.e. not simply a single parent. Comparable plating experiments have shown an incidence of such types (though not so certainly from single cells) of about 2-3% of total, ~~so it is not certain that the choice of cells has been~~ appreciably better than chance. I think that it has, however, since the data include a large proportion of unselected isolates. I would say (subjectively) that selection on basis of size has been more productive than from pairs, but as the initial pairing had been probably already completed, this does not mean too much. The 11 useful isolates have been as follows (P1= F- parent, P2= Hfr parent [in toto!], R1 = the Lac+S<sup>r</sup> recombinant, V<sub>1</sub> also segregating not recorded here), the content of the single-cell clones being:

- A 3: P1 + P2 (occasional R1, rare, and ascribed to subsequent recombination)
- B 3: P1 + P2 + R1 (the latter too frequent to be ascribed to "leakage".)
- C 5: P1 + R1. (recombinants other than Lac+S<sup>r</sup> not found, though in A and B the entire P2 genotype was certainly in the same cell).

I would conclude that an intact nucleus is transferred from the Hfr to the F- cell by the previous mating process and that, as in yeast (cf. Powell, J. Inst. Brewing, 1951) a dikaryon is initially formed, from which is obtained either a zygote (i.e. C, with added complication of segmental elimination, and possible residue of additional) or the segregation of the dikaryon (A) or, after preliminary division of the Hfr nucleus, both (B).

I am now about ready to begin attempts at defining the earlier steps of the mating along the lines of Winge's first work with yeast [which for comparative purposes, Prof. Rubbo and I are also retracing]. This promises to be a slow task, and I suspect your visit will coincide with the most active phase of it, for which we will certainly enjoy your collaboration at somewhat closer hand than before!

Your travel plans fit very well with ours. We are hoping to spend August, perhaps a week in September, at Woods Hole to use the library (and confer with Sonneborn with whom we have been discussing a comprehensive monograph on microbial genetics, whose actual writing is however far distant). We will certainly be back at Madison by Sept. 15, probably somewhat before. The semester begins about that time and I will be giving my course (two or three lectures a week) at that time. Lab. space is being saved for your visit and, as with your stipend, I think you and your wife can be comfortably, but not luxuriously, situated. But while a certain amount of actual working together will be essential, I think it more important to use the opportunity for the reconciliation and development of our ideas.

With a gratifying anticipation of this Fall,

Yours,

Joshua Lederberg